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Synthesis And Evaluation Of Anti Inflammatory Activity Of Novel Derivatives Of 2 Aminothiazole and Oxadiazole

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ABSTRACT: *Novel 2- Aminothiazole with oxadiazole derivatives were synthesised by the reaction of 2 Aminothiazole with ethylchloroacetate in the presence of potassium carbonate and Chloroform to form Compound 1 . Compound 1 on condensation with hydrazine hydrate in the presence of ethanol afforded compound (2). Compound (2) on condensation with aromatic aldehydes yielded compounds (3a-e).All these compounds were Schiff bases. Finally the Schiff bases were cyclised in the presence of Chloramine T to form a series of derivatives of 2 Aminothiazole with Oxadiazole(4a-e).The synthesised compounds were screened for their anti-inflammatory and anti microbial potential .Among them the compounds 4a and 4b have shown anti-inflammatory activity while compounds 4d and 4e has shown significant anti microbial activity.*

KEYWORDS: *2 Aminothiazole, Oxadiazole, Antiinflammatory activity, Schiff Base, Anti microbial*

I. INTRODUCTION

Aminothiazole derivatives possess various types of biological activities including anti-microbial, anti-inflammatory ,anticonvulsant and anti HIV properties. The synthesis of 1,3,4 oxadiazole is of considerable interest due to their various biological activities. Reported among these activities were anti-inflammatory , nervous system depressing , analgesic, herbicidal , antimicrobial, anticonvulsant and antitubercular properties.Our research has focused on the incorporation of the oxadiazole moiety into aminothiazole based upon the hypothesis that this modification would improve efficacy ,since both these moieties were noted for their anti-inflammatory and antimicrobial potential. Thus a series of novel derivatives of 2 Aminothiazole and Oxadiazole were synthesised and tested for their antimicrobial and anti-inflammatory potential.

II. EXPERIMENTAL

Melting points of the synthesised compounds were determined by open capillary method and were uncorrected. The IR spectra of the synthesised compounds were recorded in potassium bromide pellet discs on Jasco FTIR Spectrophotometer . The H NMR spectra of the synthesised compounds were recorded in DMSO using AV-300 BROKE JEOL Spectrophotometer and Tetramethyl Silane (TMS) was used as an internal standard. All reagents were of commercial quality and were used without further purification. The reactions progress was monitored by thin- layer chromatography (TLC)using silica gel G and spots were visualised with iodine.

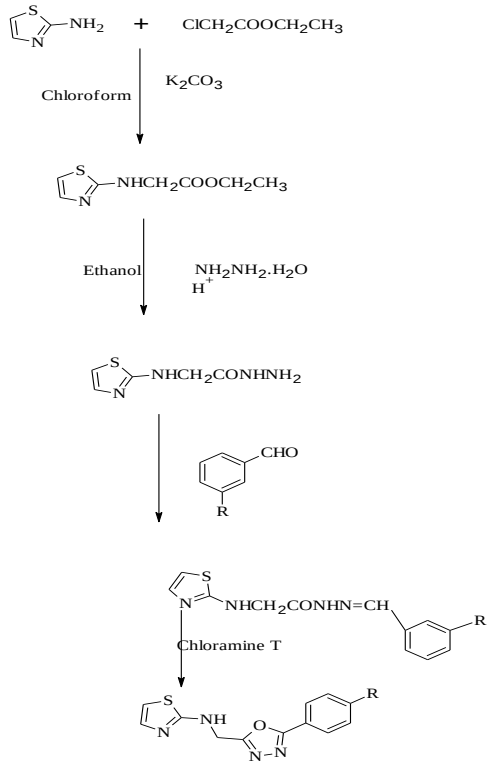
III. CHEMISTRY

Synthesis of Ethyl (1,3 Thiazolidin -2-yl- aminoacetate) (1): To a solution of recrystallised thiazolamine 1,3 diamine (1 gram,0.05 mole) in chloroform (20ml) was mixed with ethylchloroacetate (7.9 ml, 0.04 mol) and potassium carbonate (6.8 g, 0.12 mol) and refluxed for 2 hours. The completion of the reaction was monitored by Thin Layer Chromatography. The reaction mixture was filtered. From the clean filtrate, excess chloroform was removed by concentrating the solution. The resulting liquid was deep orange in colour. On recrystallisation white needle like crystals were formed. **:C7H10N2O2S,** White needle like crystals, m.p-70-72 degree Celsius,Rf:0.4 (n-hexane,ethylacetate) IR: KBr (µ cm)- 3690.12 (Heteroaromatic NH stretch),3713.26 (Amine NH Stretch),2992.06 (Heteroaromatic CH stretch),1729.83(C=O ester Stretch),1089.69 (C-O ester stretch),1630.52 (C-S Stretch),1557.24 (C-C Stretch in ring.

Synthesis of 1-(Hydrazinyloxy)-2 (1,3-Thiazolidin-2-yl amino) Ethanone

A mixture of(1) and hydrazine hydrate in Ethanol was refluxed on a water bathe for two hours . The concentrated liquid was cooled in ice cold condition . White needle like crystals began to separate out. The mixture was poured in cold Sulphuric acid, where white precipitate was formed and finally the precipitate was washed with ice cold water and dried.The resulting product was buff coloured and finally the product was recrystallised from Ethanol.

C8H18N4O5, White powdered flakes, mp: 235 degree Celsius, Rf: 0.7 (n hexane,toluene), IR: (KBr) µ cm-(Heteroaromatic NH stretch),3749.9, 3733.51 (Amine NH stretch),3202.22 (NH Stretch),1625.7 (C=O Amide stretch),1224.83 (CN Stretch)



Synthesis of Schiff Base

General Procedure: A mixture of (2a) and different aromatic aldehydes or heterocyclic aldehydes in ethanol was refluxed in the presence of few drops of glacial acetic acid in a round bottom flask on a water bathe for 2-3 hours. The reaction mixture was cooled and solid thus separated was filtered (3a), washed with ice cold water and recrystallised from ethanol.

MF:C13H13N4OS, Molecular weight: 273.3335,mp : 305 degree Celsius, Rf- 0.6 (n hexane, toluene), IR KBr (µ) cm Heteroaromatic (NH Stretch)= 3929.25, Secondary Amine (NH Stretch)= 3732.55,Aromatic(C- C Ring stretch)= 1624.73,Out of Plane (C-H Stretch) = 668.214

SYNTHESIS OF OXADIAZOLE DERIVATIVE FROM THE SCHIFF BASE.

Procedure : A solution of Schiff Base in Ethanol was refluxed with Chloramine T at room temperature for 2- 3 hours under anhydrous condition . The reaction mixture was filtered and poured into crushed ice and stirred well. The solid thus separated out was washed with water and recrystallised from Ethanol.

4A	Bromosalicylaldehydederivative
4B	Nitrobenzaldehydederivative
4C	Chlorobenzaldehydedehyde derivative
4D	Anisaldehyde derivative
4E	Furfuraldehyde derivative

MF : C13H12N4O2S, mp: 315 degree Celsius, Rf: 0.6 (nhexane, toluene),IR Kbr (µ cm) : Heteroaromatic NH Stretch (3942.75), Amine NH stretch (3926.6), Oxadiazole (C=N Stretch)=1624.73,(1640-1560), 1012 (1030-1020).

IV. RESULTS AND DISCUSSION

The structures of all compounds have been established on the basis of spectral data analysis. The appearance of primary amino group band at 3405cm/s in the IR spectrum,the NMR signal for thiazole at ð 7.8 and oxadiazole at 8.2the molecular ion peak at m/z 312.3 and fragmentation peaks at m/z 175 and 133 confirms the formation of (4a-e).1a was confirmed by the appearance of peaks at 1729 and 1089 cm. 2a was confirmed by the formation of peak at 1629 followed by the disappearance of the peak at 1729 . Schiff bases (3a-e) was formed by the appearance of an imine NH Stretch at 3732.55 and finally products(4a-e) was confirmed to have an oxadiazole moiety by the appearance of peaks at 1624.73 and 1012.

Anti inflammatory screening

All the synthesised compounds were tested for their anti-inflammatory activity using THP1 Human monocytic cell lines. The assay of inhibition of cycloxygenase enzyme was determined spectrophotometrically with the help an anti-inflammatory agents aspirin being used as control. Of the five synthesised compounds 4a,4b,4c in different concentrations exhibited considerable inhibition of cycloxygenase enzyme.

The inhibition is given in the table mentioned below

Sample concentraton(µg/ml)	**OD at 632nm**	**% inhibition**
Control	0.2590	
Sample1		
100 µg/ml	0.0843	67.45
500 µg/ml	0.0671	73.78
1000 µg/ml	0.0401	84.51
Sample2		
100 µg/ml	0.1539	40.57
500 µg/ml	0.1178	54.51
1000 µg/ml	0.0792	69.42
Sample3		
100 µg/ml	0.0924	67.26
500 µg/ml	0.0819	68.37
1000 µg/ml	0.0567	78.10

V. ACKNOWLEDGEMENT

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